Listing of the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method for prenatal diagnosis of chromosomal abnormality in a predetermined DNA region comprising the steps of : a) obtaining a plasma sample from a pregnant female; b) enriching fetal DNA regions in the plasma sample by digesting DNA from said plasma sample with an enzyme that selectively and substantially completely digests the maternal DNA to obtain a [[DNA]] sample enriched for fetal DNA regions; and c) determining the paternal or maternal allele frequency in the sample enriched for fetal DNA using polymorphic markers adjacent to or within the fetal DNA regions in the sample enriched for the fetal DNA regions of step (b), wherein a difference in allele frequency from other than 50% of paternal and 50% of maternal allele as compared to a normal control, which does not comprise a chromosomal abnormality is indicative of a chromosomal abnormality.

2. (Original) The method of claim 1, wherein the DNA is isolated from the plasma sample before it is digested.

3. (Original) The method of claim 1, wherein comparing the paternal or maternal allele frequency of step (c) is performed against at least one internal control located in a chromosome, duplication or deletion of which is not a target of diagnosis, and wherein both maternal and paternal alleles are present in equal amount, wherein deviation of the ratio from the internal control indicates presence of chromosomal abnormality.

4. (Original) The method of claim 1 further comprising a DNA amplification step performed after step (a) and before step (c).

5. (Original) The method of claim 1, wherein said enzyme of step (b) is a methyl-sensitive enzyme.

6. (Original) The method of claim 5, wherein said methyl-sensitive enzyme digests only at DNA recognition sites that are unmethylated and wherein the maternal or paternal allele, frequency is determined using polymorphic markers adjacent to or within methylated fetal DNA regions.

7. (Original) The method of claim 3, wherein said methyl-sensitive enzyme digests only at DNA recognition sites that are methylated, and wherein the maternal or paternal allele frequency is determined using polymorphic markers adjacent to or within unmethylated fetal DNA regions.

8. (Currently amended) A method for prenatal diagnosis of chromosomal abnormality comprising the steps of : a) obtaining a plasma sample from a pregnant female ; b) enriching fetal nucleic acid regions in the plasma sample by digesting nucleic acids present in said plasma sample with a methyl-sensitive enzyme that digests only unmethylated DNA; c) optionally isolating undigested enriched fetal nucleic acid regions from step (b); d) amplifying the undigested enriched fetal nucleic acid regions from step (b) or (c) while using a nucleic acid methylase to methylate nascent hemi-methylated nucleic acid; e) digesting the amplified nucleic acid of step (d) with a methyl-sensitive enzyme that digests only unmethylated nucleic acid; and f) determining the paternal or maternal allele frequency in the enriched fetal nucleic acid regions using polymorphic markers adjacent to or within unmethylated fetal nucleic acid regions, wherein a difference in allele frequency other than 50% of maternal and 50% of paternal is indicative of a chromosomal abnormality.

9. (Original) The method of claim 8, wherein the comparing of the paternal or maternal allele frequency of step (f) is performed against to a control nucleic acid sample, wherein a difference of other than the ratio in the control sample is indicative of a chromosomal abnormality.

10. (Original) The method of claim 8, wherein the nucleic acid is DNA.

11. (Original) The method of claim 8, wherein the nucleic acid is isolated from the plasma sample before it is digested.

12. (Original) The method of claim 1 or 8, wherein the chromosomal abnormality is DNA duplication.

13. (Original) The method of claim 1 or 8, wherein then chromosomal abnormality is a DNA deletion.

14. (Original) The method of claim 1 or 8, wherein the chromosomal abnormality is aneuploidy.

15. (Original) The method of claim 14, wherein said aneuploidy is selected from the group consisting of trisomy 21, trisomy 18, and trisomy 13.

16. (Currently amended) A method of diagnosing fetal chromosomal abnormality comprising the steps of : a) obtaining a plasma sample from a pregnant female; b) enriching fetal nucleic acid regions in the plasma sample by selectively treating said plasma sample to enrich the plasma sample for at least one fetal nucleic acid region; c) determining [[the]] a paternal or maternal allele frequency in the enriched fetal nucleic acid sample using at least one polymorphic marker adjacent to or within the at least one enriched fetal nucleic acid region in the sample of step (b); and d) comparing the paternal or maternal allele frequency of step (c) to a control DNA sample, wherein a difference in allele frequency from other than 50% of paternal and 50% of maternal allele is indicative of a fetal chromosomal abnormality.

17. (Currently amended) A method of diagnosing fetal chromosomal abnormality comprising the steps of : a) obtaining a plasma sample from a pregnant female; b) enriching fetal nucleic acid regions by selectively treating said plasma sample to enrich the sample for at least one fetal nucleic acid region; c) determining the paternal or maternal allele frequency using at least one polymorphic marker adjacent to or within the at least one fetal nucleic acid region in the sample enriched for fetal nucleic acid regions of step (b); and d) comparing the paternal or matemal allele frequency in the enriched

fetal nucleic acid regions of step (c) to a control DNA sample wherein the maternal and paternal alleles are present in predetermined amounts, wherein a difference in allele frequency from other than 50% of paternal and 50% of maternal allele as compared to the control is indicative of a chromosomal abnormality.

18-21. (Canceled)